COCCIDIA (SPOROZOA)

MALARIA

- **Etiology:**

  Four *Plasmodium* species are responsible for human malaria; these are

- *P. falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.

:Epidemiology

There are an estimated 200 million worldwide cases of malaria leading a mortality of more than one million people per year.

P. falciparum (malignant malaria)

P. malariae (quartan malaria) are the most common species of malarial parasite and are found in Asia and Africa.

P. vivax (benign tertian malaria) predominates in Latin America, India and Pakistan.

P. ovale (ovale tertian malaria) is almost exclusively found in Africa.

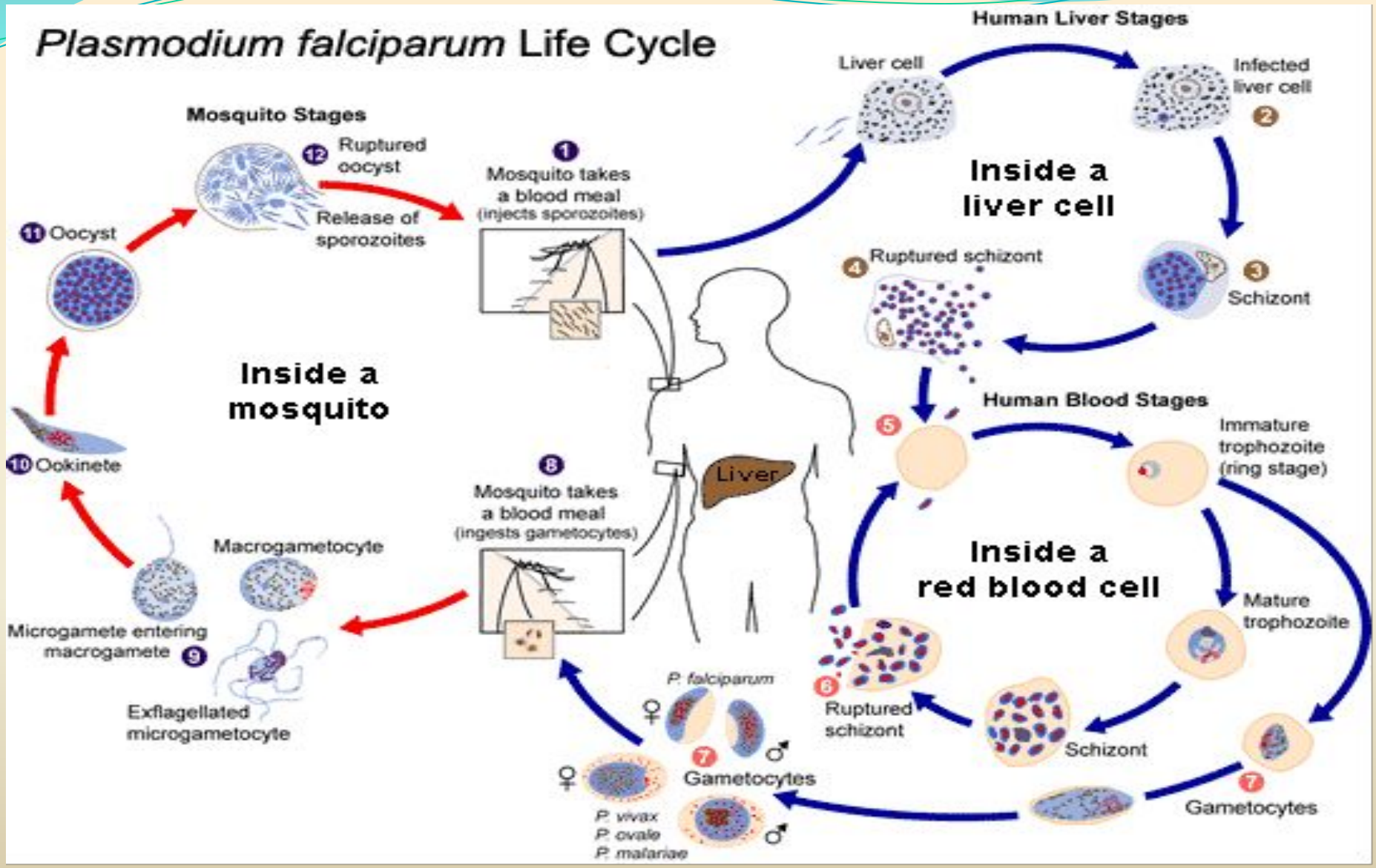
Life cycle:

The life cycle passes in three stages:

Two in man:- Exo- erythrocytic schizogony

-Erythrocytic schizogony

One in mosquito – Sporogony


Plasmodium falciparum Life Cycle
Human Liver Stages
Liver cell
Infected liver cell
2
Inside a liver cell
Mosquito Stages
12 Ruptured oocyst
Release of sporozoites
1 Mosquito takes a blood meal (injects sporozoites)
11 Oocyst
4 Ruptured schizont
3 Schizont
Inside a mosquito
Human Blood Stages
5
Immature trophozoite (ring stage)
10 Ookinete
8 Mosquito takes a blood meal (ingests gametocytes)
Liver
Macrogametocyte
Inside a red blood cell
Mature trophozoite
Microgamete entering macrogamete 9
Exflagellated microgametocyte
P. falciparum
6 Ruptured schizont
Schizont
7 Gametocytes
7 Gametocytes
P. vivax
P. ovale
P. malariae

There are two forms of sporozoites:

-----tachysporozoite and bradysporozoite

They are genetically distinct at the time of maturation when they enter the hepatic cells at the same time. tachysporozoite grow in the hepatic cell and multiply to form exoerythrocytic schizonts and then invade RBCs to clinic malaria. Bradysporozoite is the cause of relapse of malaria. Bradysporozoite stay in the hepatic cells and will multiply later.

Plasmodium falciparum

- *Plasmodium falciparum* demonstrates no selectivity in host erythrocytes, i.e. it invades young and old RBCs cells. The infected red blood cells also do not enlarge and become distorted.
- • Multiple trohpozoites can infect a single erythrocyte, and show multiple infections of cells with small ring forms.
- • The trophozoite is often seen in the host cells at the very edge or periphery of cell membrane.
- • Occasionally, reddish granules known as **Maurer's dots** are observed
- • Mature (large) trophozoite stages and schizonts are rarely seen in blood films, because their forms are sequestered in deep capillaries, liver and spleen.
- **.** Peripheral blood smears characteristically contain only young ring forms and occasionally crescent shaped gametocytes

- ***Plasmodium vivax***

- *P.vivax* is selective in that it invades only young immature erythrocytes.
- Infections of *P. vivax* have the following characteristics:
- • Infected red blood cells are usually enlarged and contain numerous pink granules or **schuffner's dots.**
- • The trophozoite is ring-shaped but amoeboid in appearance.
- • More mature trophozoites and erythrocytic schizonts containing up to 24 merozoites are present.
- • The gametocytes are round

- ***Plasmodium malariae***

- *P.malariae* can infect only mature erythrocytes with relatively rigid cell membranes.
- As a result, the parasite's growth must conform to the size and shape of red blood cell.
- This requirement produces no red cell enlargement or distortion, but it results in distinctive shapes of the parasite seen in the host cell, "band and bar forms" as well as very compact dark staining forms.
- The schizont of *P.malariae* is usually composed of eight merozoites appearing in a rosette

- **Symptoms:**
- The symptoms of malaria depends on the **parasitemia, the presence of the organism in different organs and the parasite burden**. The incubation period varies generally between 10-30 days. As the parasite load becomes significant, the patient develops headache, lassitude (tiredness), vague pains in the bones and joints, chilly sensations and fever.
- **As the disease progresses**, the chills and fever become more prominent. The chill and fever follow a cyclic pattern paroxysm (fit) with the symptomatic period lasting 8-12 hours.
- **In between** the symptomatic periods, there is a period of relative normalcy, the duration of which depends upon the species of the infecting parasite. This interval is about 34-36 hours in the case of *P. vivax* and *P. ovale* (tertian malaria), and 58-60 hours in the case of *P. malariae* (quartan malaria). Classical tertian paroxysm (fit) is rarely seen in *P. falciparum* and persistent spiking or a daily paroxysm is more usual. The malarial paroxysm is most dramatic and frightening

- **It begins** with a chilly sensation that progresses to teeth chattering, overtly shaking chill and peripheral vasoconstriction resulting in cyanotic lips and nails (cold stage). This lasts for about an hour.
- **At the end** of this period, the body temperature begins to climb and reaches 103-106 degrees F (39- 41degrees C).
- **Fever** is associated with severe headache, nausea (vomiting) and convulsions.
- The patient experiences euphoria, and profuse perspiration and the temperature begin to drop. Within a few hours the patient feels exhausted but symptom-less and remains symptomatic until the next paroxysm. **Each paroxysm is due to the rupture of infected erythrocytes and release of parasites**.

process

----to shows a succession of 3 stages

⑴.The cold stage (chill), lasting for 30 min to 1 hr.

⑵.The hot stage (fever), 1 to 4 hrs.

(3).Sweating stage 1 to 2 hrs.

Characteristic

----(1).periodic

(2).repeated

(3).regular

Without treatment, all species of human malaria may finally result in natural cure except with *P. falciparum* which becomes more severe progressively and results in death. This organism causes sequestration of capillary vasculature in the brain, gastrointestinal and renal tissues. Chronic malaria results in splenomegaly, hepatomegaly and nephritic syndromes.

- During pregnancy malaria can lead to premature baby delivery or delivery of a low-birth-weight baby. The infant can get the parasite from the mother and develop the disease. Central nervous system involvement (cerebral malaria) can cause (especially in small children) blindness, deafness, speech difficulty, paralyses and trouble with movements

Relapse

----a specific attack that it is up to months or even years after the primary attacks.

----The bradysporozoites in the liver spend a rest and sleeping times of months or even years , then they start develop in exoerythrocytic stage and erythrocytic stage. at this time, the patient occurs paroxysm , showing as periodic fever like the primary attacks, it is called relapse.

----Relapse only occurs in ***P.v.***

Malignenat Malaria

Malaria caused by P.f. is more severe than that caused by other plasmodia.

----The serious complication of P.f. involves cerebral malaria (involving the brain); massive haemoglobinuria (blackwater fever) in which the urine becomes dark incolor, because of acute hemolysis of RBC; acute respiratory distress syndrome; severe gastrointestinal symptoms; shock and renal failure which may cause death.

- **Pathology and immunology**

- Symptoms of malaria are due to the release of massive number of merozoites into the circulation. Infection results in the production of antibodies which are effective in containing the parasite load. These antibodies are against merozoites and schizonts. The infection also results in the activation of the reticuloendothelial system (phagocytes). The activated macrophages help in the destruction of infected (modified) erythrocytes and antibody-coated merozoites. Cell mediated immunity also may develop and help in the elimination of infected erythrocytes. Malarial infection is associated with immunosuppression.

Pathogenicity

- Paroxysm (attack of malaria)

mechanism

----liberation of merozoites and malarial pigment; RBC debris into the blood stream.

symptoms (in a typical case)

----p.v. attack occurs once every other day (48 hours); P.f./36 to 48 hrs ;P.m./72 hrs

Splenomegaly and anemia•

----Rupture of the infected RBCs and destruction of normal RBCs enhance phagocytosis

stimulate phagocytes to grow in number and enhance in function. Finally, lead to anemia and enlargement of the spleen.

Question: Which reasons are there in the anemia of malaria?

Diagnosis

Diagnosis is based on symptoms and detection of parasite in Giemsa stained blood smears. There are also antibody tests.

Laboratory diagnosis

----laboratory diagnosis of malaria is confirmed by the demonstration of malarial parasites in the blood film under microscopic examination.

- Thin film
- Thick film

Question: Which stages are there in the blood film of P.v. or P.f. ?

- **Treatment and Control**

- Treatment is effective with various quinine derivatives (quinine sulphate, chloroquine, meflaquine and primaquine, etc.). Drug resistance, particularly in *P. falciparum* and to some extent in *P. vivax* is a major problem.
- Control measures are eradication of infected anopheline mosquitos. Vaccines are being developed and tried but none is available yet for routine use

Treatment

- **Chlorquine and quinine**----anti-erythrocytic stage drugs. (question: Which stage of plasmodium can these drugs kill?)
- **Primaquine and pyrimethamine** ----anti-exoerythrocytic stage drugs.

Prevention

- **Chemoprophylaxis**

-----Chloroquine / pyrimethamine

used for

prophylaxis of malaria

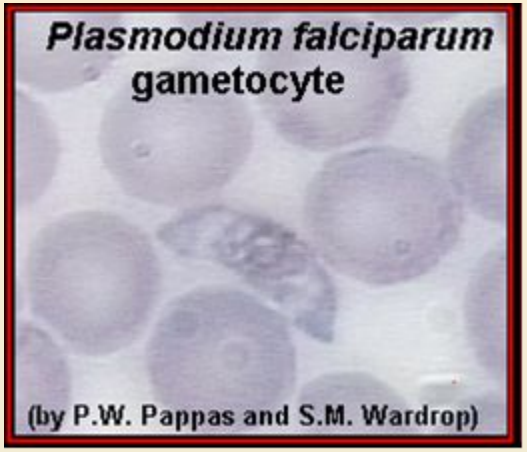
-----Chemotherapy: 1 week before entry into the endemic area ; for 4 weeks after returning from the endemic area.

Mosquito control

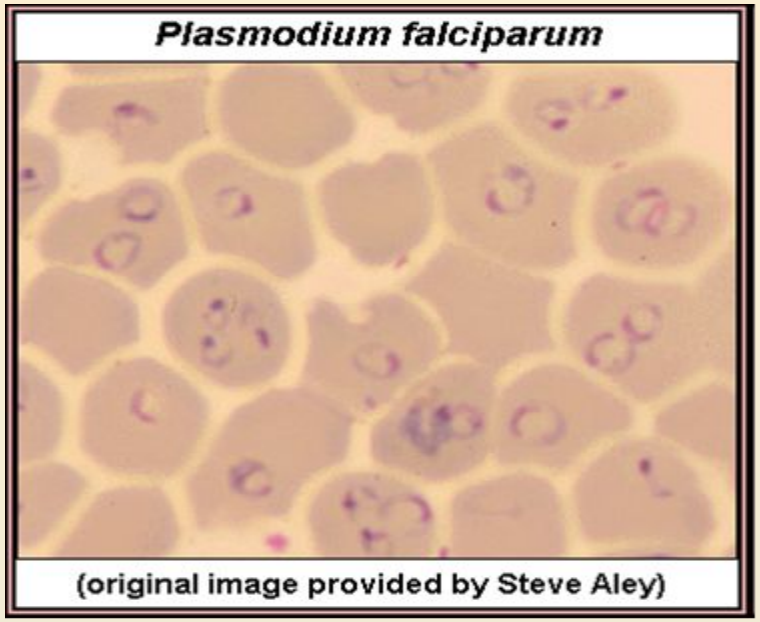
(1). Reconstruction of environment: eradicate the breeding places of moquitoes.

(2). Spry insecticides: DDVP and so on.

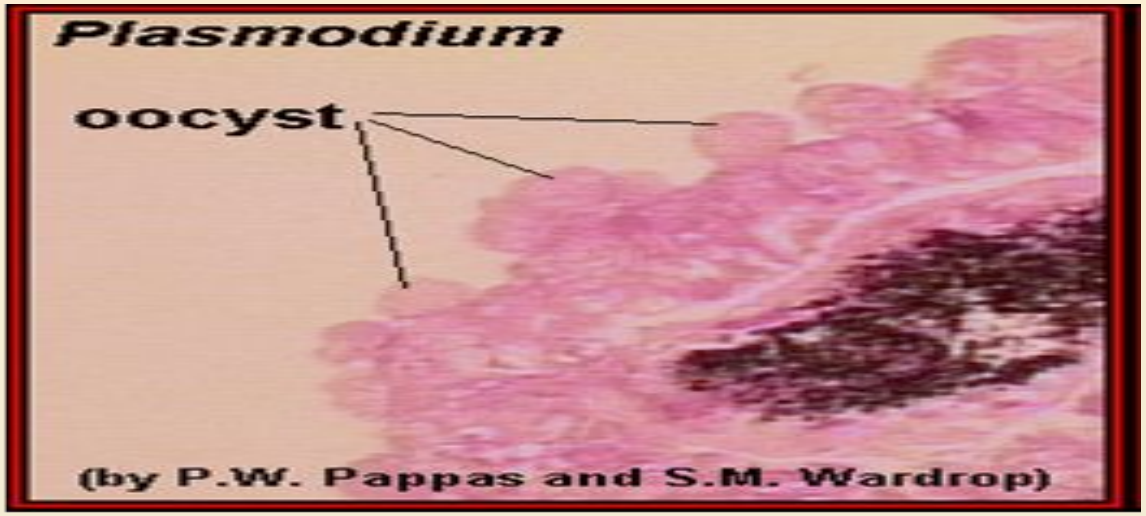
(3). Use mosquito nets, screen, or mosquito repellents to protect the person from mosquito bites.



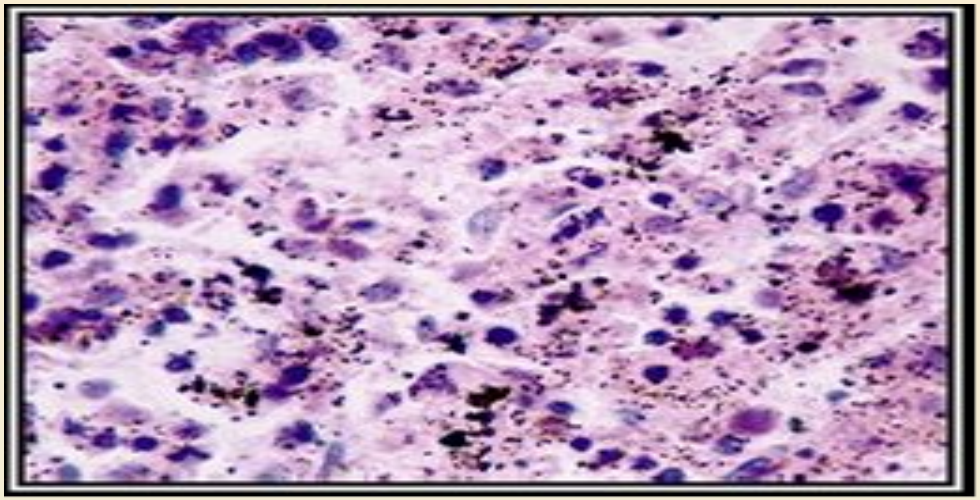
- Gametocytes of *Plasmodium falciparum* in a blood smear. Note the characteristic shape



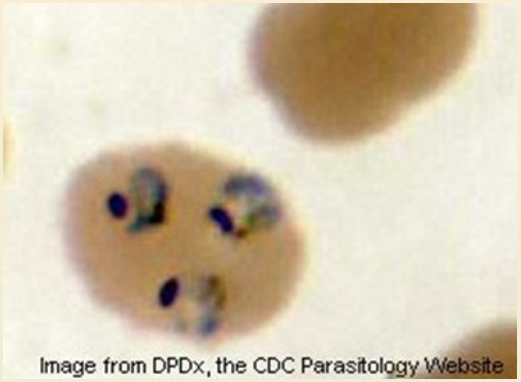
Ring stages of *Plasmodium falciparum*. Note the multiple infections of some cells.



Oocysts of *Plasmodium* on the surface of a mosquito gut. The dark material is partially digested blood inside of the mosquito gut.

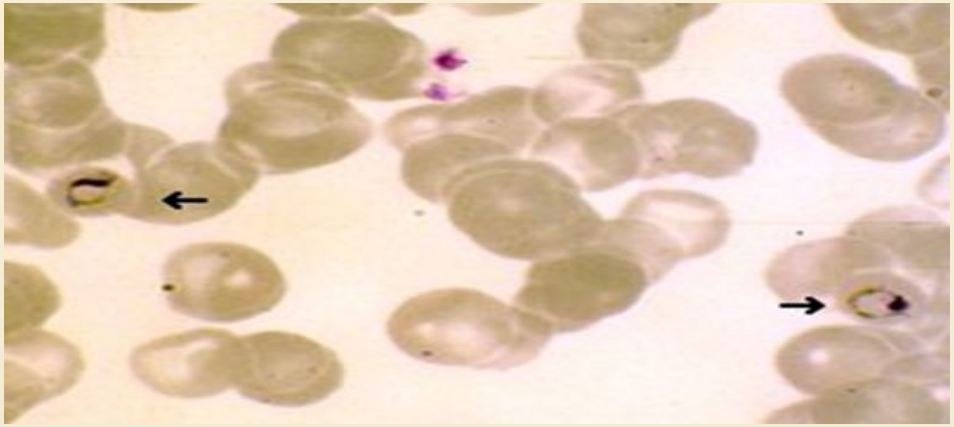


Hemozoin (digested hemoglobin) deposited in the cells of the spleen in a human infected with malaria.

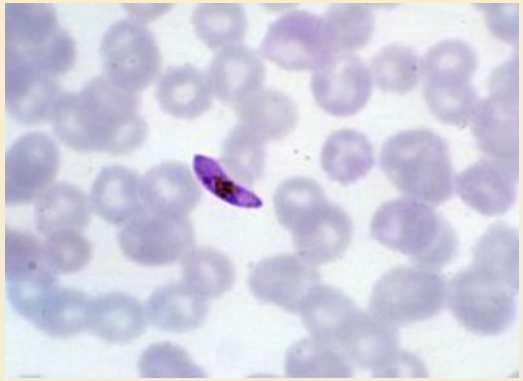


Trophozoites - *Plasmodium falciparum*: Early trophozoites have the characteristic signet ring shape. Also, unique to *P. falciparum* is the presence of multiple trophozoites in one cell.

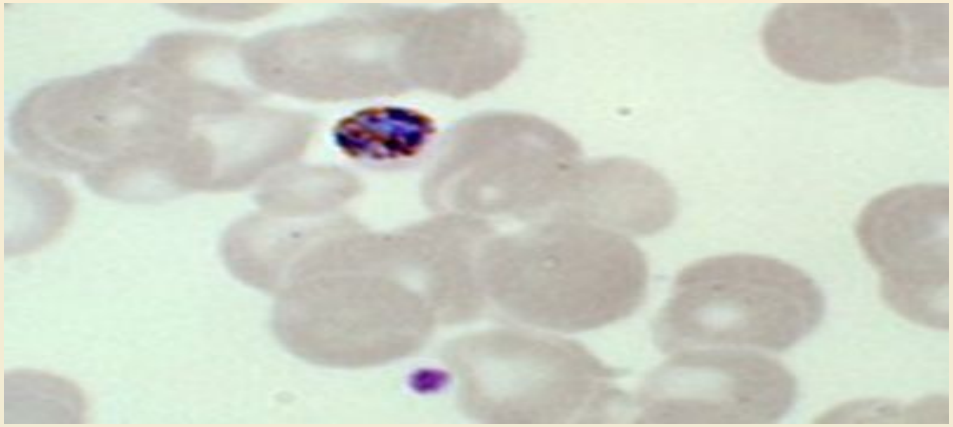
Trophozoites - *Plasmodium vivax*: Red blood cells infected by *P. vivax* are often larger than uninfected red blood cells. They approximately .1.5 times the size of a normal cell



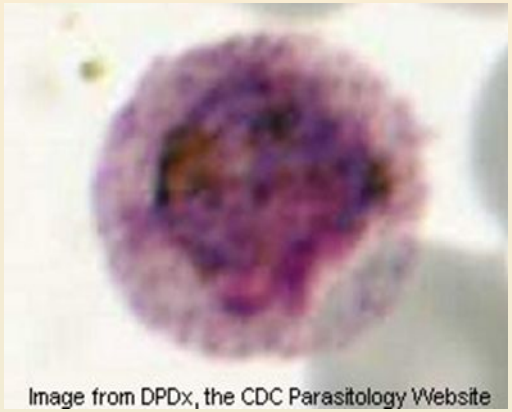
Trophozoites – *Plasmodium malariae*: Characteristic trophozoites of *P. malariae* showing the ring shape and the tendency of infected cells to be of normal or smaller size (arrows).



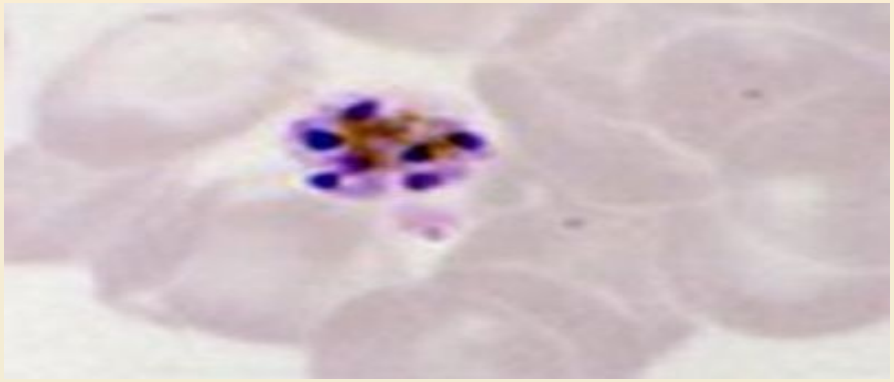
Gametocyte - *Plasmodium falciparum*: The gametocytes of *P. falciparum* have a crescent or banana shape.



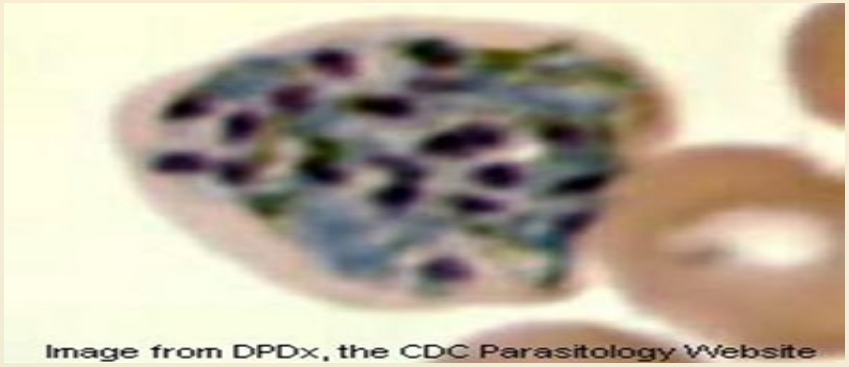
Gametocyte - *Plasmodium malariae*: The gametocytes of *P. malariae* have a round shape about the size of red blood cells. They have a fine granular appearance.



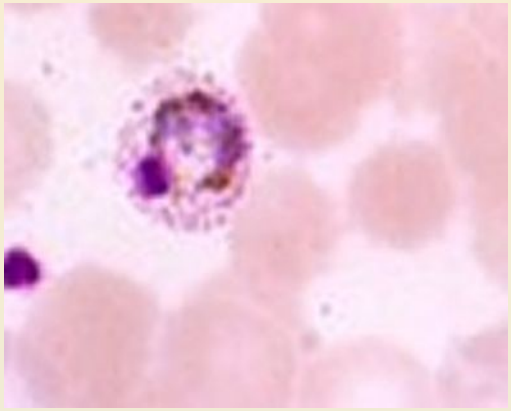
Gametocyte - *Plasmodium ovale*: A round gametocyte that is larger than normal red blood cells. It has a granular appearance as well as Schuffner's dots.



Schizont - *Plasmodium malariae*: A schizont containing merozoites (6 to 12) giving a coarse granular appearance.



Schizont - *Plasmodium vivax*: A schizont showing the large number of merozoites typical of this species (16-24). Also note the larger size compared to a normal red blood cell.



A red blood cell showing the Schuffner's dots characteristic of cells infected by *Plasmodium vivax* and *Plasmodium ovale*.